REMARKS

In view of the above amendments and following remarks, reconsideration of the outstanding office action is respectfully requested. Pursuant of 37 CFR § 1.121, attached as Appendix A is a Version With Markings to Show Changes Made.

Interactions between bacterial pathogens and their plant hosts generally fall into two categories: (1) compatible (pathogen-host), leading to intercellular bacterial growth, symptom development, and disease development in the host plant; and (2) incompatible (pathogen-nonhost), resulting in the hypersensitive response, a particular type of incompatible interaction occurring, without progressive disease symptoms. During compatible interactions on host plants, bacterial populations increase dramatically and progressive symptoms occur. During incompatible interactions, bacterial populations do not increase, and progressive symptoms do not occur.

The hypersensitive response is a rapid, localized necrosis that is associated with the active defense of plants against many pathogens. The hypersensitive response elicited by bacteria is readily observed as a tissue collapse if high concentrations ($\geq 10^7$ cells/ml) of a limited host-range pathogen like *Pseudomonas syringae* or *Erwinia amylovora* are infiltrated into the leaves of nonhost plants (necrosis occurs only in isolated plant cells at lower levels of inoculum). The capacities to elicit the hypersensitive response in a nonhost and be pathogenic in a host appear linked. These pathogens also cause physiologically similar, albeit delayed, necroses in their interactions with compatible hosts. Furthermore, the ability to produce the hypersensitive response or pathogenesis is dependent on a common set of genes, denoted *hrp*. Consequently, the hypersensitive response may hold clues to both the nature of plant defense and the basis for bacterial pathogenicity.

The *hrp* genes are widespread in gram-negative plant pathogens, where they are clustered, conserved, and in some cases interchangeable. Several *hrp* genes encode components of a protein secretion pathway similar to one used by *Yersinia, Shigella*, and *Salmonella* spp. to secrete proteins essential in animal diseases. In *E. amylovora, P. syringae*, and *P. solanacearum*, hrp genes have been shown to control the production and secretion of glycine-rich, protein elicitors of the hypersensitive response.

The first of these proteins was discovered in *E. amylovora* Ea321, a bacterium that causes fire blight of rosaceous plants, and was designated harpin. Mutations in the encoding *hrpN* gene revealed that harpin is required for *E. amylovora* to elicit a hypersensitive response in nonhost tobacco leaves and incite disease symptoms in highly

susceptible pear fruit. The *P. solanacearum* GMI1000 PopA1 protein has similar physical properties and also elicits the hypersensitive response in leaves of tobacco, which is not a host of that strain. However, *P. solanacearum popA* mutants still elicit the hypersensitive response in tobacco and incite disease in tomato. Thus, the role of these glycine-rich hypersensitive response elicitors can vary widely among gram-negative plant pathogens.

Other plant pathogenic hypersensitive response elicitors have been isolated, cloned, and sequenced. These include: *Erwinia chrysanthemi*; *Erwinia carotovora*; *Erwinia stewartii*; and *Pseudomonas syringae* pv. *syringae*.

The present invention is a further advance in the effort to identify and characterize hypersensitive response elicitor proteins.

The rejection of claims 1-2 and 47-48 under 35 U.S.C. § 112 (2nd para.) for indefiniteness, is respectfully traversed in view of the above amendments.

The rejection of claims 1-2 and 47-48 under 35 U.S.C. § 102(b) as anticipated by WO 98/54214 ("Laby") is respectfully traversed.

As stated by the U.S. Patent and Trademark Office ("PTO"), Laby "teaches an isolated hypersensitive response elicitor protein from *Erwinia amylovora* (p.19, lines 25-28) wherein the protein elicits a hypersensitive response in plants (p.6, lines 30-33), is recombinant (Ex. 2 and claims 15 and 20), and wherein the protein is comprised of the amino acids 1 through 218 of the amino acid sequence for the hypersensitive response elicitor protein from *Erwinia amylovora*" (pages 3-4, December 31, 2002, office action). The PTO has apparently taken the position this fragment contains two hypersensitive response domains as claimed in the present invention.

The accompanying Declaration of Zhong-Min Wei Under 37 CFR § 1.132 ("Wei Declaration") clearly demonstrates that the PTO's position is incorrect.

The present invention is directed to the discovery that hypersensitive response eliciting domains include two subunits (Wei Declaration ¶ 5). The first subunit, the acidic portion, has at least 10 amino acids and a pI below 5 (Id.). This acidic portion has a secondary structure in the form of a beta-sheet, a beta-turn, or an unordered form (Id.). The second subunit also has at least 10 amino acids and a secondary structure in the form of a stable alpha-helix (Id.). Neither the acid portion nor the alpha-helix subunit is independently sufficient to elicit the hypersensitive response in plants (Id.). Both subunits must be present for a hypersensitive response eliciting domain to elicit the hypersensitive response in plants (Id.).

HrpN, from *Erwinia amylovora*, is a hypersensitive response elicitor protein of 403 amino acids in length (Wei Declaration ¶ 6). Two hypersensitive response eliciting domains were identified within the native HrpN protein (Id.). The hypersensitive response eliciting domains span from amino acid 32 through 74 and from amino acid 157 through 180 (Id.).

A protein comprising amino acid sequence 1 through 218 of the amino acid sequence from the hypersensitive response elicitor HrpN from *Erwinia amylovora* would simply represent a fragment of the native full-length HrpN protein (Wei Declaration ¶ 7). The HrpN fragment would comprise the two identified hypersensitive response eliciting domains (amino acid sequence 32-74, "first domain" and amino acid sequence 157-180, "second domain"), as well as the native flanking amino acid sequence 1 through 31, immediately preceding the first domain, amino acid sequence 75 through 156, immediately following the first domain and immediately preceding the second domain, and amino acid sequence 181 through 218, immediately following the second domain (Id.).

The hypersensitive response eliciting domains present in the protein comprising amino acid sequence 1 through 218 of the amino acid sequence from the hypersensitive response elicitor HrpN, are in a native form (Wei Declaration ¶ 8). The domains are present amongst the native flanking amino acid sequences, in their native orientation, such that would be found in the naturally occurring HrpN elicitor protein from *Erwinia amylovora* (Id.).

In contrast, the protein of the present invention requires one or more domains which are isolated from all other regions of the native hypersensitive response elicitor protein from which the domain originated. Thus, domains adjacent to the acidic portion linked to an alpha-helix in Laby's 1-218 amino acid protein fragment are clearly excluded from claim.

Accordingly, applicants respectfully submit that the rejection of claims 1-2, 47- 48 under 35 U.S.C. § 102(b) as anticipated by Laby is improper and should be withdrawn.

In view of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450, on the date below.
Date 6/25/03 | Wendy L. Barry

Appendix A

Version With Markings to Show Changes Made

In reference to the amendments made to claim 1, additions appear as underlined text, while deletions appear as bracketed text, as indicated below:

In the Claims:

Claim 1 has been amended as follows:

1. (Amended) A protein which elicits a hypersensitive response in plants, said protein comprising one or more hypersensitive response eliciting domains, wherein each domain is comprised of an acidic portion linked to an alpha-helix, said acidic portion having at least 10 amino acids and a pI below 5, said one or more domains being isolated from all other regions of a native hypersensitive response elicitor protein from which the domains originated[An isolated hypersensitive response elicitor protein comprising an isolated pair or more of spaced apart domains, each comprising an acidic portion linked to an alpha-helix and capable of eliciting a hypersensitive response in plants].